UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
ADDRESS: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/400,492	09/21/1999	KENNETH RHODES	MNI-069CP	3470

959 7590 11/19/2002

LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/400,492	RHODES ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,12,15-21,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 2* is/are allowed.

6)☒ Claim(s) *3,11,12,15-21,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/12/2002 has been entered.

Formal Matters

Claim 22 was cancelled and claims 1, 3, 17, 18 and 19 were amended in Paper No. 20, 9/12/2002. Claims 1-3, 11-12, 15-21, 23-24 are pending and under consideration.

Response to Arguments and Amendment

Applicant's arguments filed in Paper No. 20, 9/12/2002 have been fully considered, but they are persuasive in part.

The rejection of claims 1-2 under 35 USC § 112 first paragraph has been obviated by Applicant's amendment, and are thus withdrawn.

The rejection of claims 1-3, 11-12, 15-16 under 35 USC § 102 has been obviated by Applicant's amendment, and are thus withdrawn.

The rejection of claims 1-3, 11-12 and 15-23 under 35 USC § 112 second paragraph are indefinite in that they only describe the peptide of interest by an arbitrary protein name, i.e. "PCIP" has been obviated by Applicant's amendment, and is thus withdrawn.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-3, 11-12, 15-16 has been applied to new claims 17-23, which are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a compound suitable for treatment wherein the PCIP is 9q, does not reasonably provide enablement for a method of identifying a compound suitable for treatment wherein the polypeptide is a fragment of PCIP 9q, for reasons of record set forth in Paper No. 11, 8/9/2001. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record argues that the indicated claims are overly broad in the recitation of "fragments". There is not adequate guidance as to the nature of the fragments which Applicants claim. There is insufficient guidance provided in the specification as to the relationship between the structure of PCIP 9q and its function. Without this information, it would require undue experimentation for one of skill in the art to practice a method of identifying a compound suitable for treatment wherein the polypeptide is a fragment of PCIP 9q.

Applicant has added the limitation "biologically active" to attempt to better define the function of the fragments of PCIP 9q. There is insufficient guidance as to the nature of the fragments which Applicants claim. There is insufficient guidance provided in the specification as to the relationship between the structure of PCIP 9q and its function. Without this information, it

would require undue experimentation for one of skill in the art to practice a method of identifying a compound suitable for treating a cardiovascular disorder comprising contacting a biologically active fragment of 9q PCIP, other than that which is exemplified in the specification.

Claims 17-23 are directed to a method of identifying a compound suitable for treating a cardiovascular disorder comprising contacting a biologically active fragment of 9q PCIP. In the specification (page 18, lines 35-36), Applicants disclose that biologically active fragments of the PCIP protein can be identified by a method used for determining direct binding, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible fragments of PCIP 9q.

However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. There is insufficient guidance provided in the instant specification as to how one of ordinary skill in the art would practice a method of identifying a compound suitable for treating a cardiovascular disorder comprising contacting a biologically active fragment of 9q PCIP. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The Wands Court set forth eight factors to consider in the determination of whether a disclosure does not satisfy the enablement requirement and would require undue experimentation. The relevant factors in the instant case are set forth below:

(1) the nature of the invention - the claimed invention is a method of identifying a compound suitable for treating a cardiovascular disorder comprising contacting a biologically active fragment of 9q PCIP, or at least 10 amino acids of PCIP 9q.

(2) the state of the prior art - it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

(3) the level of one of ordinary skill the Mikayama and Voet disclosures is evidence that one of ordinary skill in the art would have difficulty practicing the claimed method.

(4) the level of predictability in the art - the Mikayama and Voet references are evidence that the level of predictability in making making functional protein fragments is low.

(5) the amount of direction provided by the inventor - the specification has provided insufficient guidance to practice a method of identifying a compound suitable for treating a cardiovascular disorder comprising contacting a biologically active fragment of 9q PCIP.

(6) the existence of working examples - no working examples are provided.

(7) the quantity of experimentation needed to make or use the invention based on the content of the disclosure - Testing and screening the vast collection embraced by the claimed subject matter for functional activity would clearly require undue experimentation. For example, SEQ ID NO: 14 is 270 amino acids long. To make and test all of the fragments of SEQ ID NO: 14, even those containing 10 contiguous amino acids, would require the production of many polypeptides, and Applicants fail to provide any *a priori* basis, short of making and testing all possible combinations, that would allow one to distinguish operative embodiments from inoperative embodiments.

Given the disclosure of Mikayama and Voet, it would require undue experimentation to practice a method of identifying a compound suitable for treating a cardiovascular disorder comprising contacting a biologically active fragment of 9q PCIP.

There is insufficient guidance provided in the specification as to how one of ordinary skill in the art would to practice a method of identifying a compound suitable for treatment wherein the polypeptide is a fragment of PCIP 9q other than those exemplified in the specification.

Applicant argues that ample guidance and working examples are provided to determine the functional significance of the various domains of the PCIP 9q polypeptides. However, as set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without

> difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. In the instant case, the claimed invention is a method of identifying a compound suitable for treating a cardiovascular disorder comprising contacting a biologically active fragment of 9q PCIP, or at least 10 amino acids of PCIP 9q. Given the unpredictability of the protein art, and that only a few of the sequences that meet the functional limitations of the claim are disclosed, it would require undue experimentation to make and use the claimed invention.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
November 14, 2002